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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,577	02/23/2004	Lung-Ji Chang	58416-00005	9914

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K&L Gates LLP
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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
04/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/785,577	CHANG, LUNG-JI	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-20,51 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20,51 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The request for continued examination filed February 12, 2009 has been entered. The amendment filed February 12, 2009 (hereinafter referred to as "the response") has been entered. Claim 17 has been amended and Claims 51 and 52 have been newly added.

Accordingly, Claims 17-20, 51, and 52 are pending in the instant application

The elected invention is drawn to a tumor cell composition comprising a tumor cell modified to express a B7-2 protein and at least one additional immune modulator, or a functional fragment of said B7-2 protein or said immune modulator. Applicants further elected GM-CSF as the cytokine species for prosecution.

Accordingly, Claims 17-20, 51, and 52 are examined herein.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 12, 2009 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-20, 51, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,548,068 (Schlom et al., priority to 6/7/95) and Dranoff et al. (1993, Proc. Natl. Acad. Sci. USA 90: 3539-3543).

The claims are directed to a tumor cell composition consisting of an isolated primary tumor cell modified to express a B7-2 protein and at least one additional immune modulator, wherein said isolated primary tumor cell expressing B7-2 and at least one immune modulator has been irradiated. Dependent claims further specify that the immune modulator is a cytokine and that the cytokine is GM-CSF. Claim 52 is directed to a tumor cell composition comprising an isolated autologous primary tumor cell transfected to express a B7-2 protein and GM-CSF, wherein said isolated autologous primary tumor cell expressing B7-2 and GM-CSF has been irradiated.

Schlom et al. disclose and claim a tumor cell modified to express B7-2 and GM-CSF. See especially Claims 1, 4, and 5. Claim 1 is directed to a host cell infected with a recombinant vaccinia virus which has incorporated into the viral genome a gene or portion thereof encoding B7-2. The claim further specifies that the B7-2 gene is expressed. Claim 4 is directed to the host cell according to Claim 1 wherein the recombinant virus further comprises one or more genes or portion thereof encoding an immunostimulatory molecule selected from the group consisting of IL-2, ICAM-1, LFA-3, CD72, GM-CSF, TNFα, INFγ, IL-12, IL-6 and combinations thereof. Claim 5 is directed to the host cell according to any one of Claims 1 to 4 "wherein the host cell is …a tumor cell …" Thus, the patent clearly discloses a tumor cell modified to express both B7-2 and GM-CSF, as instantly claimed. The reference further discloses that the recombinant vaccine composition may be used for gene therapy and that such an approach requires using cells from a given patient, inserting a gene encoding an immunostimulatory molecule such as B7-1, B7-2, IL-2, or GM-CSF into those cells, and administering the cultured cells back to the patient (column 1, lines 40-45). Thus, the patient receives genetically-modified autologous cells which minimizes or eliminates immunorejection of the introduced cells. This approach clearly discloses

the production of an isolated primary tumor cell modified to express a B7-2 protein and at least one additional immune modulator, as instantly claimed.

Dranoff et al. (1993) disclose that irradiated tumor cells expressing murine GM-CSF stimulated potent, long-lasting, and specific anti-tumor immunity (abstract). With regard to the use of autologous cells, the reference further states that "the use of autologous cancer cells as vaccines to augment anti-tumor immunity has been explored throughout this century" (page 3539, column 1, paragraph 1). With regard to the use of irradiated cells and primary tumor cells, the reference further teaches "to the extent that either the *in vitro* manipulation of tumor cells or retroviral integration might pose the risk of conferring a more malignant phenotype upon the transduced cells, the use of irradiated rather than live cells as cancer vaccines would appear to be extremely important. Moreover, since primary tumor explants likely contain nonneoplatic elements as well, irradiation of the tumor samples before vaccination will also prevent the possibility of the autonomous growth of nonneoplastic cells induced by autocrine synthesis of their own growth factors" (page 3543, column 1, paragraph 2).

Given that Dranoff et al. teaches a distinct advantage to using irradiated primary tumor cells rather than live cells as cancer vaccines, one of skill in the art would have been clearly motivated to irradiate the tumor cell compositions of Schlom et al. to avoid the risk of introducing cells with a malignant phenotype and to avoid the growth of nonneoplastic cells that may be present in a composition produced from a primary tumor explant.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

At page 5 of the response, Applicanst assert that Schlom does not disclose isolated primary tumor cells that have been modified to express B7-2 proteins and at least one additional immune modulator, wherein the isolated primary tumor cell expressing B7-2 and at least one additional immune modulator has been irradiated. However, Dranoff et al. (1993) teaches this limitation and the distinct advantage of

using irradiated primary tumor cells rather than live cells as cancer vaccines. Accordingly, the argument is moot in view of the rejection under 35 U.S.C. 103.

At page 6 of the response, Applicants assert that Schlom is not enabling for isolated primary tumor cells that have been modified to express B7-2 proteins and at least one additional immune modulator, wherein the isolated primary tumor cell expressing B7-2 and at least one immune modulator. Applicants continue to argue that Schlom discloses that tumor cells "expressing both the tumor associated antigen along with an immunostimulatory molecule are administered to a mammal in an effective amount to result in tumor reduction or elimination in the mammal afflicted with cancer" (citing column 13, line 64 to column 14, line 4 of Schlom). Applicants further contend that Schlom does not provide any specific examples of such tumor cells containing these components or of their use as immunogenic compositions. However, reduction to practice is not required to enable the disclosed tumor cell compositions, as transduction of tumor cells with recombinant virus encoding the B7-2 and GM-CSF proteins is fully enabled given the advanced state of the art for transducing cells with viral vectors. Furthermore, the composition claims are issued in a U.S. Patent and therefore are understood to be fully enabled.

Conclusion

No claims are allowable.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632